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EXAMINER
SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,123	LI ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,54 and 56-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,54 and 56-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/2006 (indicating the amendments filed 5/10/2006) has been entered.

2. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Sitton.

3. Currently, claims 1, 3, 54, 56, and newly added claims 57-63 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Upon review of the instant specification, the following objections and rejections are either newly applied or are maintained. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow, where appropriate. This action is NON-FINAL.

New Grounds of Rejection and Objection

Specification

4. The submission filed 4/24/2002 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: on 4/24/2002, in response to a NOTICE to file Missing Parts, a Sequence listing was filed. The specification discloses a "SEQ ID NO: 1" at page "76". However, this version of 'SEQ ID NO: 1", which is 2021 nucleotides long, is not identical to the sequence disclosed as SEQ ID NO: 1, which is 1818 nucleotides long, in the sequence listing filed 4/24/2002. The specification provides no basis for the SEQ ID NO: 1 in the sequence listing. The submission filed 4/24/2002 was reviewed, but it appears that the sequence listing was filed without a statement attesting that no new matter was disclosed, nor a statement that the paper copy and the computer readable form are the same.

Applicant is required to cancel the new matter in the reply to this Office Action.

5. The disclosure is objected to. Although the specification appears to consist of only 69 pages, the specification appears to end at page 68. After page 68, there is a page designated as "76" which recites the sequences of a nucleic acid sequence, which is termed "SEQ ID NO: 1", as well as a protein sequence which is termed, "SEQ ID NO: 2". It is not clear, what pages 69-75 are, or whether page "76" is intended to be part of the specification, or a figure. It is not referred to in the "Brief Description of the drawings". Additionally, both the nucleotide sequences at pages 36-37, and that at page "76" are noted as "The GenBank entry NM_003620",

however the sequences are NOT the same. The sequence which is at pages 36-37 is SEQ ID NO: 3 in the sequence listing which is 2973 nucleotides long, while "SEQ ID NO: 1" at page "76" is 2021 sequences long. The disclosure is therefore unclear. Appropriate correction is required, however applicant should take care not to enter New Matter in correcting the discrepancy.

Claim Rejections - 35 USC § 112

6. Claims 1, 3, 54, and 56-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "a WIP1 gene having a nucleotide sequence of nucleotides 1-1818 of SEQ ID NO: 1 or of nucleotides 1-2973 of SEQ ID NO: 3". The term "having" is considered open, for example, as "comprising". This transitional terminology allows for additional elements on either side of the indicated SEQ ID NO:, but not additional sequences in the middle. However, the sequences of SEQ ID NOS: 1 and 3 appear to be coding sequences, without introns. However, a gene normally includes introns, and it appears that the WIP1 gene has introns (see previous dbSNP report, which designates exonic polymorphisms in reference to a genomic contig. The SNPs are spaced more than 2973 nucleotides apart, in different exons). Accordingly, it is unclear how a WIP1 gene can "comprise" or "have" the indicated SEQ ID NOS, which are CDS and exclude introns, and still be a "gene".

7. Claims 1, 3, 54, and 56-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite SEQ ID NO: 1, with positions 1-1818, however the specification provides no basis or guidance for this designation. As noted in the specification objection above, the version of SEQ ID NO: 1, which was filed after the filing date of the instant application, does not correspond to the sequence at page "76".

The claims recite detecting and measuring gene copy number of a WIP1 gene having a nucleotide sequence of nucleotides 1-1818 of SEQ ID NO: 1 or of 1-2973 of SEQ ID NO: 3 in lung or breast tissue. The specification points to the sequence listing for support for SEQ ID NO: 1 and 3 in the claims. As noted in above, the sequence of SEQ ID NO: 1 was not provided in the specification as originally filed. At page 64, the specification teaches a working example of detecting WIP1 amplification using microarray based CGH (comparative genomic hybridization). The specification teaches using a TaqMan probe set representing the target and a reference probe representing normal non amplified, single copy region in the genome. At page 66, the specification teaches that the inventors demonstrated that WIP1 is located at the epicenter of the amplification region using Q-PCR and fluorogenic TaqMan probes based on undisclosed EST's or BAC sequences. It is noted, however, that the specification does not teach determining the sequence of the WIP1 gene that was amplified. Accordingly, while the specification teaches that the WIP1 gene is present in the amplified region, the specific sequence of the WIP1 gene is

not taught (considering that SNPs are known to exist in the gene, see dbSNP printout). Therefor, while the specification teaches that SEQ ID NO: 3 is the sequence found in a particular accession number from GenBank, it does not teach that the sequence of the gene which was found to be amplified in Tables 1 and 2, or at pages 64 or 66, is SEQ ID NO: 1 or SEQ ID NO: 3. Accordingly, the specification does not appear to provide support for the claims as written.

Additionally, claim 60 has been amended to recite that gene copy number is determined by real time quantitative RT-PCR. However, while the specification provides support for detecting expression changes using RT-PCR, the specification teaches that expression level changes of a gene are not necessarily correlative of changes in gene copy number. The specification does not appear to provide support for measuring gene copy number using RT-PCR.

8. Claims 1, 3, 54, and 56-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims are broadly drawn to a method of diagnosing *any* precancerous lesion or *any* cancer in by detecting and measuring the gene copy number of a WIP1 gene "having" a nucleotide sequence of nucleotides 1-1818 of SEQ ID NO: 1 or 1-2973 of SEQ ID NO: 3, in breast or lung tissue sample from a human that is suspected to be precancerous or cancerous, thereby generating data for a test gene copy number; and comparing the test gene copy number to data for a control gene copy number, wherein *any* amplification of the gene in the lung or breast tissue indicates the presence of a precancerous lesion or a cancer in the human.

The amount of direction or guidance:

The specification teaches that the detection of amplified or overexpressed oncogenes is an important method for diagnosing cancer (page 4). The specification teaches that gene amplification involves a chromosomal region bearing specific genes undergoing a relative increase in DNA copy number, thereby increasing the copies of any genes that are present (page 3, first para). However the specification also teaches that the overexpression of certain well known genes, such as c-myc, have been observed at fairly high levels in the absence of gene amplification. Accordingly, it is clear from the teachings in the specification, that detection of overexpression of a gene does not predictably correlate to increased DNA copy number of that gene. In other words, although amplification of a gene normally leads to overexpression, overexpression of a gene does not necessarily indicate that the copy number of the gene has been increased or amplified.

The specification teaches that WIP1 is a serine/threonine specific protein phosphatase type 2C (PP2C) family member whose expression is induced in response to gamma or UV radiation in a p53-dependent manner (pages 37 and 38). The specification broadly defines the WIP1 gene as WIP1 nucleic acids (DNA or RNA) that can include their polymorphic variants, alleles, mutants, and interspecies homologs that have substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry AAB61637 or SEQ ID NO:1 (pages 21 and 22). The specification also teaches that expression of WIP1 can transform normal cells into cells with a more cancerous phenotype (page 39). The specification also teaches that WIP1 is found within human chromosome 17q23, which is one of the most frequently amplified regions in human breast cancer (page 39).

The specification teaches that the WIP1 gene is amplified and/or overexpressed in several breast tumor cell lines (Table 1). The specification also teaches that the WIP1 gene is overexpressed in several primary tumor samples of different types of cancer and amplified in several primary breast tumor samples (Table 2). The specification further teaches methods for detecting and quantitating WIP1 gene amplification and level of expression (pages 40-45). These methods, however, involve hybridization analysis, which does not determine the nucleotide sequence of the entire region that is amplified.

Presence and absence of working examples:

The specification teaches that the WIP1 gene is amplified and/or overexpressed in several cell lines derived from human breast cancer tumors (Table 1). With regard to gene amplification in primary tumors, the specification teaches that the WIP1 gene is amplified in 16% of a

sampling of human breast tumors. While the specification teaches that 3% of a sampling of human lung tumors showed amplification, in actuality, only 1 out of 31 tumors showed amplification at 3.1x, where 2.5x is considered a cutoff for amplification. (Table 2 and page 40). The specification further teaches that amplification of the WIP1 gene was not found in human colon, prostate, and ovarian tumors (Table 2) and the specification is silent with respect to the amplification of the WIP1 gene in numerous other types of cancers that exist such as brain and liver cancer. The specification teaches that WIP1 was overexpressed in 8-47% of the tumors selected from breast, colon, lung, metastatic prostate, and ovary tissues and was not found overexpressed in primary prostate tumors (Table 2). The specification teaches that while WIP1 was overexpressed in 47% of the metastatic prostate tumors examined, the genomic gene itself was not found amplified in any metastatic prostate tumors (Table 2). Therefore, the teachings of the specification do not address an association of the amplification of the WIP1 gene with *any* type of cancer and the teachings with regard to the amplification of the WIP1 gene in colon, prostate, lung, and ovarian tumors indicate, in fact, that there is not an association of the amplification of the WIP1 gene with *any* type of cancer. In addition, the specification teaches that there is no predictable correlation between WIP1 overexpression and genomic gene amplification.

The specification does not teach or provide any working examples that WIP1 copy number is increased in precancerous lesions.

The specification does not teach or provide any working examples that detection of WIP1 amplification in lung or breast tissue is diagnostic for any type of cancer or precancerous lesion, as is broadly encompassed by the claims.

At page 64, the specification teaches a working example of detecting WIP1 amplification using microarray based CGH (comparative genomic hybridization). The specification teaches using a TaqMan probe set representing the target and a reference probe representing normal non amplified, single copy region in the genome. At page 66, the specification teaches that the inventors demonstrated that WIP1 is located at the epicenter of the amplification region using Q-PCR and fluorogenic TaqMan probes based on undisclosed EST's or BAC sequences. It is noted, however, that the specification does not teach determining the sequence of the WIP1 gene that was amplified. Accordingly, while the specification teaches that the WIP1 gene is present in the amplified region, the specific sequence of the WIP1 gene is not taught (considering that SNPs are known to exist in the gene, see dbSNP printout). Accordingly, as the specification does not teach the sequences of the probes used for CGH or the EST's or BAC sequences which were used to construct the probes, nor provide the skilled artisan with the ability to identify the specific samples of tumor tissue that were used in the analysis, the skilled artisan would be unable to predictably determine which specific sequence was amplified in the specification, let alone one that contained the sequences listed in the claims.

The state of the prior art and the predictability or unpredictability of the art:

Several studies have examined the association of amplification and overexpression of the WIP1 gene with different types of cancer. These studies reveal that the art is unpredictable with regard to an association of the amplification of the WIP1 gene with various types of cancer. Kansai et al. teach that Wip1 is not expressed at higher levels in human stomach, colorectal, or hepatocellular cancers compared to corresponding non-cancerous tissues, suggesting that the

WIP1 genomic gene is not amplified in these cancers (see Kanai, et. al., (2001), *J. Cancer Res. Clin. Oncol.*, vol. 127, Table 3). In addition, Bulavin et al. teach that *PPM1D* (WIP1) is amplified and overexpressed in human breast cancer cell lines BT-474 and MCF7 but not in other breast cancer cell lines NCI-ADR and MDA-N or in cell lines derived from kidney carcinomas (ACHN) or T-cell leukemias (Molt4) (see Bulavin, et. al., (2002), *Nat. Gen.*, vol. 31, Figure 4). Furthermore, the collective teachings of the specification and the art teach that the frequency of amplification of the WIP1 gene varies in different cancers, such as breast and ovarian cancers, and therefore the skilled artisan would not be expected to reproducibly diagnose a cancer in a particular tissue (such as ovarian cancer) by analyzing the amplification of the WIP1 gene in tissue from a disparate organ (such as the breast).

The level of skill in the art:

The level of skill in the art is deemed to be high.

The quantity of experimentation necessary:

Based on the limited guidance in the specification, and the unpredictability taught in the art, it would require undue experimentation for one of skill in the art to practice the invention as it is broadly claimed. The skilled artisan would have to test an association between the amplification of the WIP1 gene in lung or breast tissue with different types of cancer by testing an exhaustive list of different types of cancers and different precancerous lesions to establish whether detection of any level of amplification in lung or breast tissue as compared to a control sample was diagnostic of any cancer or precancerous lesion. With regard to lung cancer, the

specification teaches that only 1 out of 31 lung tumor samples showed amplification near threshold levels. The detection of a single sample, at a level near threshold (3.1 vs 2.5 threshold), is not predictably indicative that amplification of WIP1 in lung tissue is predictably diagnostic of any cancer or precancerous lesion, including lung cancer. Further, the claims are drawn to a gene with specific nucleotide sequences which encode the WIP1 protein. However, it is known that SNPs occur in the coding sequence of WIP1, while the specification does not teach the specific gene sequence of WIP1 which was amplified. Accordingly, the specific sequence of the WIP1 gene which was detected in the example taught in the specification is unclear. Based on the unpredictability in the art with regard to associating overexpression of genes with specific DNA copy number increases, as well as the negative teachings in the art with regard to an association between WIP1 gene copy number increases and a number of different cancers, as well as the lack of guidance in the specification regarding the specific nucleotide sequence of the gene which was amplified, the skilled artisan would be required to perform a large amount of unpredictable trial and error analysis. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the limited amount of working examples and the negative teachings of the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one skilled in the art to perform the methods of the instant claims as written.

Response to Arguments

9. The response traverses the rejection. The response asserts that the specification teaches SEQ ID NOS 1 and 3. This argument has been thoroughly reviewed but was not found

persuasive as the specification does not teach the specific nucleotide sequence of the gene WIP1 gene which was found to amplified in breast cancer tissue, nor which specific nucleotide sequence was found to be overexpressed in the samples detected. The response asserts that the specification teaches the term cancer refers to the presence of cells possessing characteristics typical of cancer causing cells, such as uncontrolled proliferation, etc and that the term precancerous refers to tissues having characteristics relating to the changes that may lead to malignancy or cancer. This argument has been thoroughly reviewed but was not found persuasive as the specification does not teach or provide any working examples that WIP1 amplification was found in or is characteristic of precancerous lesions. The response asserts that applicants specification teaches that the claimed tissue is one that contains or is suspected of containing nucleic acids or polypeptides of WIP1 and that it teaches that increased copy number as well as RNA overexpression was observed in both breast tumor samples and lung tumor samples using TaqMan and RT-Taqman, respectively. This argument has been thoroughly reviewed but was found unpersuasive. The specification only teaches that single sample out of 31 lung tumors showed amplification (3.1) near threshold (2.5). Although table 2 shows overexpression of WIP1 in 23% of lung tumors and only 15 % of breast tumors, the specification also teaches that expression level is not necessarily correlative of amplification. For these reasons and the reasons made of record above, the rejection is maintained.

10. In the interest of compact prosecution, the following rejections are set forth.

Claim Rejections - 35 USC § 102

11. Claims 1, 2, 54, 56, 57, 61, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Kallioniemi et al. (herein referred to as Kallioniemi, *Proc. Natl. Acad. Sci. USA*, vol. 91, pages 2156-2160, 03/1994), as defined by Wu et al. (herein referred to as Wu, *Cancer Res.*, vol. 61, pages 4951-4955, 07/2001) and Genbank Accession number NM_003620 (1999, as set forth at pages 36-37 of the instant specification).

It is noted that the recitation of "...a nucleotide sequence of SEQ ID NO..." encompasses sequences from within the recited SEQ ID NO. in contrast to the recitation of "the nucleotide sequence of..."

Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 (see Figure 1 of Wu). Kallioniemi teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell lines (instant claims 1 and 2; see Tables 1 and 2, page 2156, all of paragraph 5, and page 2157, all of paragraphs 1 and 2). Kallioniemi teach that copy number increases of the 17q22-24 region were found in 18% of primary breast tumors and 67% of breast cancer cell lines examined (see Tables 1 and 2 and page 2159, paragraph 2, lines 5 and 6 of Kallioniemi). This above method taught by Kallioniemi involves comparative genomic hybridization in which the relative intensity of a fluorescent signal from a test chromosome (from tumor cells for example) hybridized with a labeled probe is compared to the intensity of a fluorescent signal from a control chromosome hybridized with the same probe that emits a different fluorescent color (instant claims 1, 54, 56, 57, 61, and 62; see page 2156, paragraph 2, lines 3-8 of Kallioniemi). Kallioniemi teaches that the probe/chromosome hybridizations of the above method were

analyzed using a digital image analysis system that was based on either a Nikon SA or Zeiss Axioplan microscope equipped with a cooled charge-coupled device camera and a filter system consisting of a triple-band-pass beam splitter and emission filters and therefore the data was stored in an electronic video format (instant claim 3; see Figure 1 and page 2157, paragraph 3, lines 1-6 of Kallioniemi). Kallioniemi further teaches that three-color images derived from the above method were processed with a Sun IPX workstation using Scil-Image software for pseudocolor display and therefore the data was analyzed via video display and compared and compiled at a location where the data was transmitted (instant claim 3; page 2157, paragraph 3, lines 11-14 of Kallioniemi).

Although Kallioniemi does not teach the sequence which is amplified, nor does Wu teach the specific sequence detected by Kallioniemi, as stated in the MPEP in chapter 2100:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the instant case, Kallioniemi teaches detecting amplification of 17q22-24 in a number of different tumors and cell lines. Thus, the office has sound basis for believing that some breast tumor samples which showed amplification of 17q22-q24 contained the gene which encoded the claimed sequences.

Response to Arguments

12. The response traverses the rejection. The response asserts that Wu et al does not prove that Kallioniemi inherently teaches amplification of nucleotides 1-1818 of SEQ ID NO: 1 or 1-2973 of SEQ ID NO: 3. This argument has been thoroughly reviewed but was found

unpersuasive. It should be noted that although the specification teaches the sequence of WIP1 of a Genbank accession number, this doesn't prove that the gene which was found to be amplified in the tumor samples in table 2 was that of the instantly claimed SEQ ID NOS. The specification does not teach the specific nucleotide sequence of the WIP1 gene which was found to be amplified.

In the instant case, Kallioniemi teaches detecting amplification of 17q22-24 in a number of different tumors and cell lines. Thus, the office has sound basis for believing that some breast tumor samples which showed amplification of 17q22-q24 contained the gene which encoded the claimed sequences. The response asserts that Kallioniemi fails to identify WIP1 as a possible candidate gene. This argument has been thoroughly reviewed but was found unpersuasive as the lack of identification of WIP1 by Kallioniemi does not exclude it from being a gene in the region amplified. The response further asserts that "it simply does not follow that Kallioniemi et al inherently teaches amplification of any WIP1 sequence" because Wu does not teach analyzing 17q24, which may contain additional genes which are amplified. This argument has been thoroughly reviewed but was found unpersuasive. The fact that additional genes may be present in the amplified region does not indicate that WIP1 is not. Further, attorney's arguments cannot take the place of evidence on the record. As stated in the MPEP, 2106 "Arguments of Counsel"

> "However, it must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See In re Budnick, 537 F.2d at 538, 190 USPQ at 424; In re Schulze, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); In re Cole, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement."

The rejection is therefore maintained.

13. Claims 1, 2, 54, 56, 57, 59, 61, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Orsetti (Orsetti et al; Oncogene, vol. 18, pages 6262-6270, 1999), as defined by Wu et al. (herein referred to as Wu, *Cancer Res.*, vol. 61, pages 4951-4955, 07/2001) and Genbank Accession number NM_003620 (1999, as set forth at pages 36-37 of the instant specification).

It is noted that the recitation of "...a nucleotide sequence of SEQ ID NO..." encompasses sequences from within the recited SEQ ID NO. in contrast to the recitation of "the nucleotide sequence of..."

Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 (see Figure 1 of Wu). Orsetti teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors, and 3 of the entire long arm (see Fig. 2, Fig 5, and para bridging cols 1 and 2 of page 6264). This above method taught by Orsetti includes PCR, FISH, and CGH (see page 6269). Orsetti teaches microscopy and digital image analysis (page 6269, fig 4).

Although Orsetti does not teach the specific nucleotide sequence which is amplified, as stated in the MPEP in chapter 2100:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the instant case, Orsetti teaches detecting amplification of 17q21-24 and 17q21-qter in a number of different breast tumors and cell lines. Thus, the office has sound basis for believing

that some breast tumor samples which showed amplification of 17q21-q24 and 17q21-qter contained the gene which encoded the claimed sequences.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claim 63 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi or Orsetti, each in view of Pinkel (Pinkel et al; Nature Genetics, vol. 20, pages 207-211, 1998).

Kallioniemi teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell lines (instant claims 1 and 2; see Tables 1 and 2, page 2156, all of paragraph 5, and page 2157, all of paragraphs 1 and 2). Kallioniemi teach that copy number increases of the 17q22-24 region were found in 18% of primary breast tumors and 67% of breast cancer cell lines examined (see Tables 1 and 2 and page 2159, paragraph 2, lines 5 and 6 of Kallioniemi). This above method taught by Kallioniemi involves comparative genomic hybridization in which the relative intensity of a fluorescent signal from a test chromosome (from tumor cells for example) hybridized with a labeled probe is compared to the intensity of a fluorescent signal from a control chromosome hybridized with the same probe that emits a different fluorescent color (instant claims 1, 54, 56, 57, 61, and 62; see page 2156, paragraph 2, lines 3-8 of Kallioniemi).

Orsetti teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors, and 3 of the entire long arm (see Fig. 2, Fig 5, and para bridging cols 1 and 2 of page 6264). This above method taught by Orsetti uses CGH (see page 6269).

Neither Kallioniemi nor Orsetti teach using microarray based CGH, however Pinkel teaches that arrays allow for high resolution analysis of DNA copy number variation using CGH. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Kallioniemi or Orsetti with the microarray based CGH method of Pinkel. The ordinary artisan would have been motivated to improve the CGH methods of Kallioniemi or Orsetti with the microarray based method of Pinkel for higher resolution analysis of DNA copy number variations.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton

Jehanne Sitton
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9/18/06